

Remarks

Claims 1-66, 94, 97-103, 110-112 and 115 have been cancelled previously. Claims 81-85 and 87-93 have been withdrawn.

Claims 67-69, 71-77, 79-80, 86, 104-109, and 113 have been previously presented. Claims 70, 78, 95, 96 and 114 are currently amended herein. Claims 116-119 are newly added herein. Thus claims 67-80, 86, 95, 96, 104-109, 113, 114 and 116-119 are being examined in the instant application.

The changes in the currently amended claims 70, 78, 95, 96 and 114 do not involve new matter, and are supported by the specification as originally filed. Applicants have removed the word "soluble" from claims 70, 78, and 95 because it is unnecessary for patentability. Applicants do not intend to surrender the subject matter claimed therein that is soluble.

Support for newly added claim 116 can be found on page 27 lines 12-17 of the specification as originally filed.

Support for newly added claim 117 can be found on page 36 line 26 through page 37 line 14 of the specification as originally filed.

Support for newly added claim 118 can be found on page 35 line 24 through page 36 line 1 of the specification as originally filed.

Support for newly added claim 119 can be found on page 35 line 24 through page 36 line 1 of the specification as originally filed.

Claims 67-80, 86, 95, 96, 104-109, 113 and 114 are rejected under 35 USC 102(b) as being anticipated by Peach et al. (WO 98/33513) as evidenced by Cohen et al. (US 2003/0083246).

Applicants traverse the rejection for the reasons of record. For the Examiner's convenience Applicants restate below, under the heading A., the arguments made in their response of November 29, 2004. Further below, under the heading B., Applicants provide new response not found in the response of November 29, 2004.

A. Restatement of response of November 29, 2004

The Patent Office acknowledges, on page 4 of the Office Action, "that WO98/33513 teaches that the sequence of LEA29Y is set forth in SEQ ID NO:1 (where Xaa is "Y" and Yaa is "E"), and that the amino acid sequence of SEQ ID NO:1 is not the same as instant SEQ ID NO:4 or the amino acid sequence set forth in instant Figure 7." The Applicants agree with the Patent Office and assert that Peach et al. (WO 98/33513), alone or as evidenced by Cohen et al., does not expressly or inherently anticipate the instantly claimed CTLA4 mutant molecules.

The Patent Office expresses concerns about the identity of the instantly claimed invention, relating to how the instantly claimed invention and a molecule in Peach et al. (WO 98/33513) have been named. Before directly addressing these concerns, the Applicants wish to direct the Patent Office to the claims being examined in the instant application. These claims, along with the disclosure in WO 98/33513, must drive the novelty analysis.

Each claim being examined in the instant application refers to a disclosed amino acid sequence and defines the CTLA4 mutant molecule being claimed by that amino acid sequence. In each claim, the claimed CTLA4 mutant molecule has two mutations in the CTLA4 extracellular domain relative to the wild type CTLA4 extracellular domain: a mutation of leucine at position 104 to glutamic acid; and a mutation of alanine at position 29 to tyrosine (using the numbering system of Figure 7 of the instant application). No claim claims a CTLA4 mutant molecule defined by a name. The term "LEA29Y" is not used in any claim. The claims clearly define the invention being claimed, and that definition is by sequence.

The Patent Office states, on page 3 of the Office Action, that "[n]o objective evidence that the LEA29Y molecule taught by Peach et al. is different [from] the instantly claimed LEA29Y molecule has been presented by the Applicant," and that "[a]bsent any factual evidence to clarify the identity of the claimed molecule, the [102(b)] rejection is maintained essentially for the reasons of record." The Applicants submit that the sequence in the instant application *is the evidence* defining an instantly claimed CTLA4 mutant molecule, and that the sequence *is the identity* of a claimed CTLA4 mutant molecule. There is no clarification needed. The Applicants submit that, equally importantly, the sequence in the

prior art reference WO98/33513 is the evidence defining a molecule in that prior art reference. To anticipate an instantly claimed molecule which is defined by sequence, a prior art molecule must have the same sequence as the instantly claimed molecule. As noted by the Patent Office, the sequences of the instantly claimed CTLA4 mutant molecules are not in the prior art of record.

The Applicants direct the Patent Office to SEQ ID NO:4 and Figure 7 of the instant application for clear factual evidence of the identity of a claimed CTLA4 mutant molecule comprising an amino acid sequence beginning with methionine at position 27 and ending with lysine at position 383 of SEQ ID NO:4 or an amino acid sequence beginning with alanine at position 26 and ending with lysine at position 383 of SEQ ID NO:4 (claim 76). Using the numbering system of Figure 7 of the instant application, this instantly claimed CTLA4 mutant molecule has a mutation of leucine at position 104 to glutamic acid, and a mutation of alanine at position 29 to tyrosine. To the contrary, using the same numbering system of Figure 7 of the instant application, the prior art Peach et al. (WO98/33513) discloses a CTLA4 mutant molecule which has a mutation at position 105 to glutamic acid, and a mutation at position 28 to tyrosine. The disclosure of the prior art reference does not contain each element of the sequence of the instantly claimed molecule and, therefore, cannot be anticipatory. ("Anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention, arranged as in the claim." *Lindermann Maschinenfabrik GMBH v. American Hoist & Derrick*, 221 USPQ 481, 485 (Fed. Cir. 1984)). Applicants assert that the instantly claimed molecules meet the legal standard for novelty.

The Patent Office, on page 3 of the Office Action, expresses confusion with the concept that a molecule can be referred to by the same name as another molecule with a different amino acid sequence. The Patent Office is unclear about how two different disclosed sequences in two different documents ended up with the same name and wishes to determine "which of the two definitions of molecular identity is correct: either (a) the same molecule is disclosed as having two different amino acid sequences in Peach et al. (WO 98/33513) and the instant application, e.g. due to a sequencing error, or (b) two different molecules have been given the same name by the same group of Inventors."

The Applicants respectfully submit that determining which of the two sequences “correctly” defines “LEA29Y” is irrelevant in determining the novelty of the instantly claimed invention. What is relevant in determining the novelty of the instantly claimed invention is what sequence was disclosed in the prior art reference and what sequence is now being claimed. A name used to refer to an invention is not important; it is the elements of the claimed invention and not the given name that defines the claimed invention. (See, eg., *Ethyl Molded Products Company v. Betts Packaging, Inc*, 9 U.S.P.Q.2D 1001, 1011 (1988) “In viewing the prior art, as well as determining infringement, the names given to parts of a closure are not important.... Thus, it is the actual structure and function of a closure part that is important, and not the name given to it by the defendant.”) Sequence defines a claimed CTLA4 mutant molecule, and, as acknowledged by the Patent Office, the prior art sequence set forth in SEQ ID NO:1 of WO98/33513 is not the same as the claimed molecule defined by instant SEQ ID NO:4 or Figure 7. Applicants assert that the instantly claimed molecules meet the legal standard for novelty.

The Patent Office states, on page 4 of the Office Action that an ordinary artisan at the time of the invention would have recognized that there was a discrepancy between the sequences set forth in SEQ ID NO:1 and Figure 7 of WO98/33513 and the description of the positions mutated in the CTLA4 sequence provided on page 19 of WO98/33513. To support this assertion, the Patent Office states that “[f]or example, page 19 identifies the CDR1 loop of CTLA4 as S25 to R33, whereas Figure 7 has S26 and R34.” The Patent Office seems to be asserting that because of this alleged discrepancy the instantly claimed invention was disclosed in WO98/33513 to the ordinary artisan. Without commenting on whether the ordinary artisan would indeed have recognized the alleged discrepancy, the Applicants respectfully disagree with the Patent Office’s basis for the rejection.

The Patent Office refers to an alleged discrepancy in WO98/33513 in the identification of the CDR1 loop, presumably relating to the mutation at position 29 from alanine to tyrosine in the instantly claimed invention. The instantly claimed invention has two mutations: one at position 29, which is in the CDR1 loop; and one at position 104, which is not in the CDR1 loop. The rejection does not address the mutation at position 104. A proper rejection addresses all elements of the claimed invention. The Applicants submit that this rejection is inadequate because all elements of the claimed invention are

not addressed. The Applicants assert that the instantly claimed molecules meet the legal standard for novelty.

B. New response

Applicants submit concurrently herewith an Information Disclosure Statement and direct the Examiner's attention to this Information Disclosure Statement and the Information Disclosure Statements submitted on June 19, 2001, January 18, 2002, March 6, 2002, May 1, 2002, June 7, 2002, November 4, 2002, June 23, 2003. Applicants and the undersigned attorney recognize their duty of disclosure under 37 C.F.R. §1.56 and submit and have submitted the aforementioned Information Disclosure Statements in accordance with that duty.

Applicants thank the Examiner for discussing this case with the undersigned attorney. Based on Applicants' understanding of the Examiner's concerns expressed in the discussion, and based on the Office Action dated September 27, 2004, Applicants provide the following.

It is clear that the *document* Peach et al. (WO 98/33513) as evidenced by the *document* Cohen et al. (US 2003/0083246) does not anticipate the claimed invention. The claimed invention simply is not disclosed on the printed pages of Peach et al. (WO 98/33513), either alone or as evidenced by Cohen et al. (US 2003/0083246). The Office recognizes this, as it states on page 4 of the Office Action "[t]he Examiner acknowledges that WO98/33513 teaches that the sequence of LEA29Y is set forth in SEQ ID NO:1 (where Xaa is "Y" and Yaa is "E"), and that the amino acid sequence of SEQ ID NO:1 is not the same as instant SEQ ID NO:4 or the amino acid sequence set forth in instant Figure 7."

Although recognizing that the claimed invention is not anticipated by the disclosures on the printed pages of the cited reference documents, the Office takes a step away from those disclosures and tries to read between the lines of the cited references, attempting to glean from the cited references when a physical embodiment of the claimed invention may have existed. The claimed invention could have existed before the priority dates, the Office imagines. The Office then takes another step that completely exits the realm of the cited reference documents. The Office hypothesizes that if a physical embodiment of the claimed invention existed before the priority dates, it or a description of it may have left the

control of the inventors and been publicly available before the priority dates -- through some means other than the clearly unanticipatory cited references.

It must be recognized that nowhere on the printed pages of Peach et al. (WO 98/33513) or Cohen et al. (US 2003/0083246) does it say or even suggest that a physical embodiment of the instantly claimed invention, or a description of it, (or, for that matter, of the invention described in Peach et al. (WO 98/33513)) was made publicly available. Thus any rejection brought concerning public availability of the claimed invention is not properly brought over the cited references.

Applicants confirm that they produced and had possession of a physical embodiment of a molecule covered by at least one claim of the instant application before the priority dates of the instant application. This is clearly evidenced in the Information Disclosure Statements.

However, it does not follow from the above facts that the claimed invention was publicly available before the priority dates of the instant application. Existence is not equal to public availability, and existence is not a bar to patentability.

Many, if not most, patent applications are filed after the applicant has produced a physical embodiment and is in possession of the claimed invention. The Examples of countless patent applications claiming compound X make clear that compound X was produced before the priority date. With respect to all such patent applications, the Office could hypothesize that the applicant may have made the claimed invention publicly available before the priority date. The law provides 37 C.F.R. §1.56 to address that hypothesis. The duty under 37 C.F.R. §1.56 ensures that the Office will be made aware of all information known to each individual associated with the filing and prosecution of the patent application to be material to patentability. In response to the Office's hypothesis, the applicant need do nothing more than meet its duty under 37 C.F.R. §1.56. This seems only fair, since the Office's hypothesis is just that -- an hypothesis, unsubstantiated speculation.

Applicants submit concurrently herewith an Information Disclosure Statement and direct the Examiner's attention to this Information Disclosure Statement and the Information Disclosure Statements submitted on June 19, 2001, January 18, 2002, March 6, 2002, May 1, 2002, June 7, 2002, November 4, 2002, June 23, 2003. Applicants and the undersigned attorney recognize their duty of disclosure under 37 C.F.R. §1.56 and submit and have

submitted the aforementioned Information Disclosure Statements in accordance with that duty.

Applicants note that the inventors of Peach et al. (WO 98/33513) and the inventors of the instant application are one in the same. Thus there is no reason to hypothesize based on Peach et al. (WO 98/33513) that another inventive entity independently produced the claimed invention before the priority dates of the instant application.

Applicants also note that there is no ATCC deposit associated with the invention of Peach et al. (WO 98/33513).

If the Office remains concerned that the claimed invention may have been publicly available before the priority dates of the instant application, Applicants respectfully request that the Office clearly raise and explain its concerns in a *prima facie*, non-final rejection. Applicants respectfully assert that any such rejection is new and must be non-final. It is not properly brought over Peach et al. (WO 98/33513) as evidenced by Cohen et al. (US 2003/0083246) because the cited references do not state or suggest that the claimed invention was publicly available before the priority dates of the instant application.

Similarly, if the Office believes that more is required of Applicants than acting in accordance with the duty under 37 C.F.R. §1.56, Applicants respectfully request that the Office clearly explain what is required and cite the relevant statutory, regulatory and/or M.P.E.P. provisions(s) that impose any such requirement.

Based upon the foregoing and the arguments previously made in Applicants' responses dated June 1, 2004 and November 29, 2004, Applicants assert that the pending claims are not anticipated under 35 USC 102(b) by the cited references.


Conclusion

Applicants respectfully request that the Patent Office withdraw the rejections under 35 U.S.C. 102(b).

The Examiner is invited to contact the undersigned if there are any questions relating to the prosecution of this application.

The Commissioner is authorized to charge Deposit Account 19-3880 (Bristol-Myers Squibb Company) for any requisite fees due or to credit any overpayment.

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